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Title of Grant: Multiscale Multiphysics Model of Thrombus Biomechanics in Aortic Dissection

Abstract Authors

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Abstract Text

The overall goal of this project is to develop a series of data-driven models to be coupled to create a novel multiscale multiphysics understanding of aortic dissection, including both the dissection process and the process of intramural thrombosis within the false lumen. A well-established murine model, the angiotensin II infused *Apoe*^{-/-} mouse, is used to collect multimodality data to inform the multiple computational models. Computer-controlled experiments and consistent validated data analysis software increased rigor and reproducibility in the data. With regard to the biomechanical models, we first developed constitutive / computational models for the normal suprarenal aorta, which is where the dissection occurs. Continuum, constrained mixture, and dissipative particle dynamics models have all been created for the normal wall and continuum and constrained mixture models have been created for the non-dissected angiotensin II infused wall. Excellent simultaneous fits to data from multiple protocols validated these constitutive models, the primary one of which was independently validated by another group (and shown to be superior to competing models). We also developed phenomenological continuum and a continuum-particle based models of thrombus formation, both again being validated by comparison to data collected in vivo using 3D ultrasound, ex vivo using optical coherence tomography, and in vitro via histology and immunohistochemistry. New co-registration techniques allow these multiple experimental data sets to be combined. Finally, we are similarly in the process of developing congruent models of the dissection process, one via a newly extended particle-continuum method and one via a phase field approach. Having multiple approaches to address the same processes enables evaluation of model congruency, which is critical since the different models are built on the same basic data but also model-specific inputs. All models are version controlled and currently archived to a lab server. This work has been documented in over 30 archival papers and described in diverse venues via invited talks by the MPIs as well as via accepted presentations by trainees, again at diverse meeting venues. We have demonstrated and emphasized in multiple publications the need for standardization not just in model development, but indeed in data collection as well. The latter has been shown, in part, via consistent comparisons of data across multiple murine models, which also provides increased insight because of the use of standardized methods.